

# Stem Cells and Stem Cell Medical Tourism

Vermont State House  
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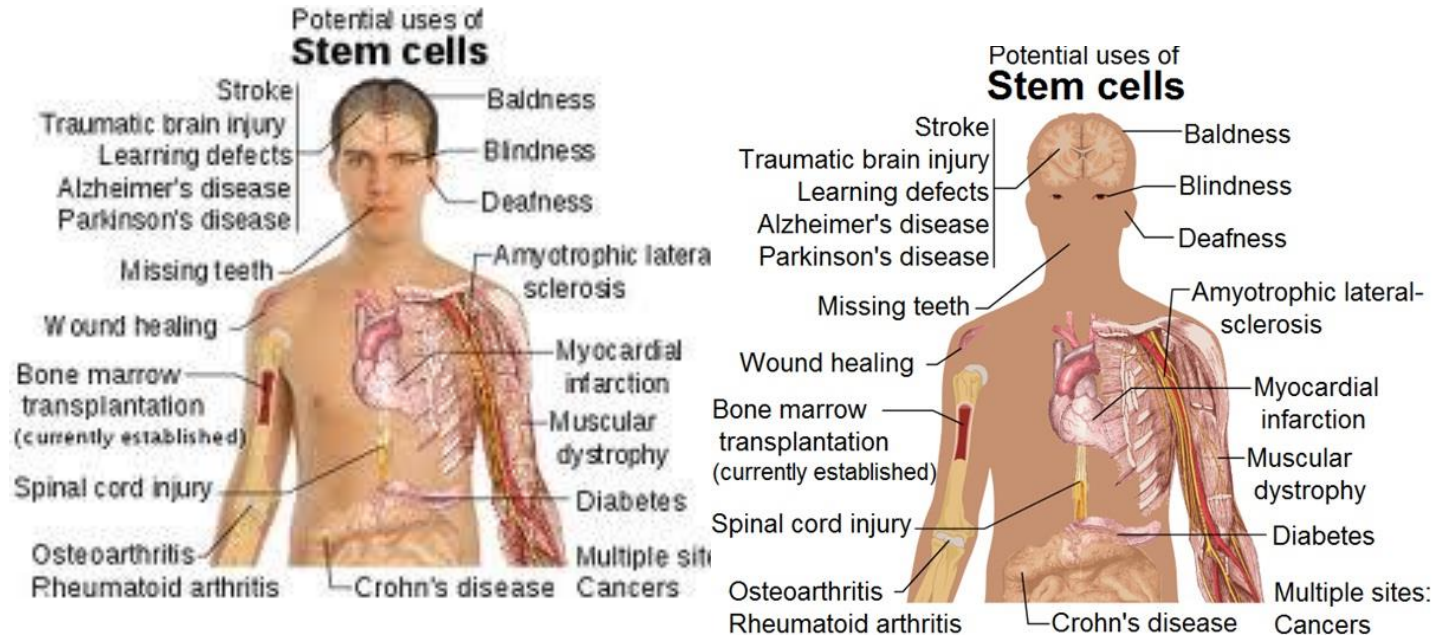
# Disclosures

- Research Funding
  - National Institutes of Health
  - Department of Defense
  - Cystic Fibrosis Foundation
  - United Therapeutics Inc.
  - Medical Technology Enterprise Consortium

# Overview

- Stem Cells
  - Embryonic and Induced Pluripotent
  - Hematopoietic (HSC)
  - Mesenchymal (MSC)
- Current FDA-approved use of stem cells
  - HSCs only: bone marrow transplantation
- Unproven, unauthorized use of stem cells
  - MSCs
  - Scope of problem
- Countering the problem

# What can you do with ESCs?



## Goal: Repair damaged or diseased tissue

### A) Administer ESCs

Go to damaged organ and differentiate into organ-specific cells

### B) Differentiate the ESCs to the desired cells or tissue in culture (directed differentiation) and then administer

Theoretically unlimited potential

## Problems with ESCs

- Ethical, moral, religious, political
- Source?
- Teratomas

Tumors containing multiple types of tissues

Skin

Muscle

Bone

Hair

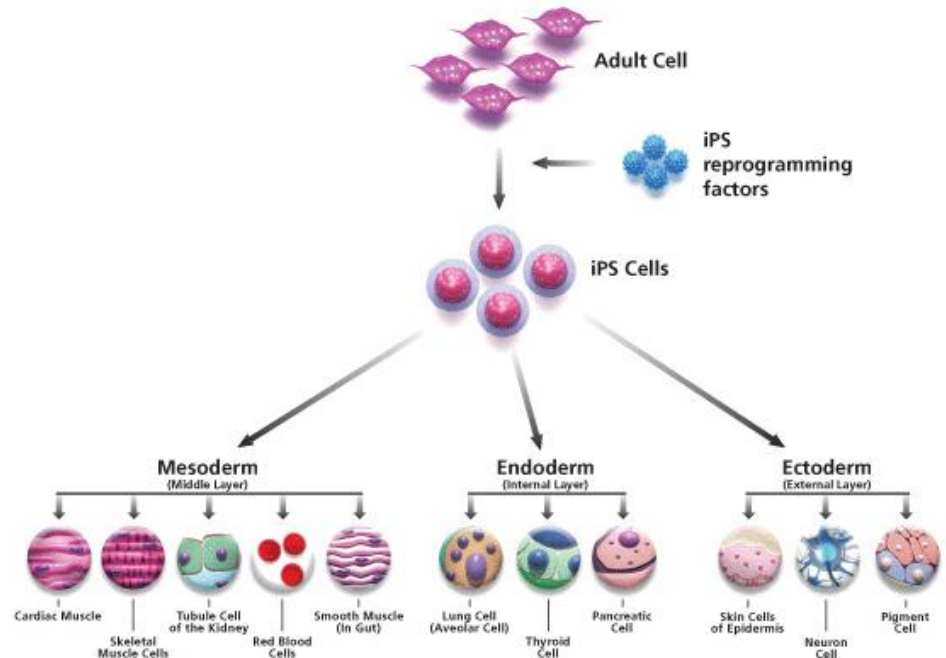
Teeth



- **Few clinical trials**
- **Many years from clinical use**
- **No approved therapies**

# Induced Pluripotent Stem Cells (iPSCs)

- Functional ESC equivalent derived from adult cells
- No ethical, religious, moral, political concerns
- Same problems: teratomas



- **Few clinical trials**
- **Many years from clinical use**
- **No approved therapies**

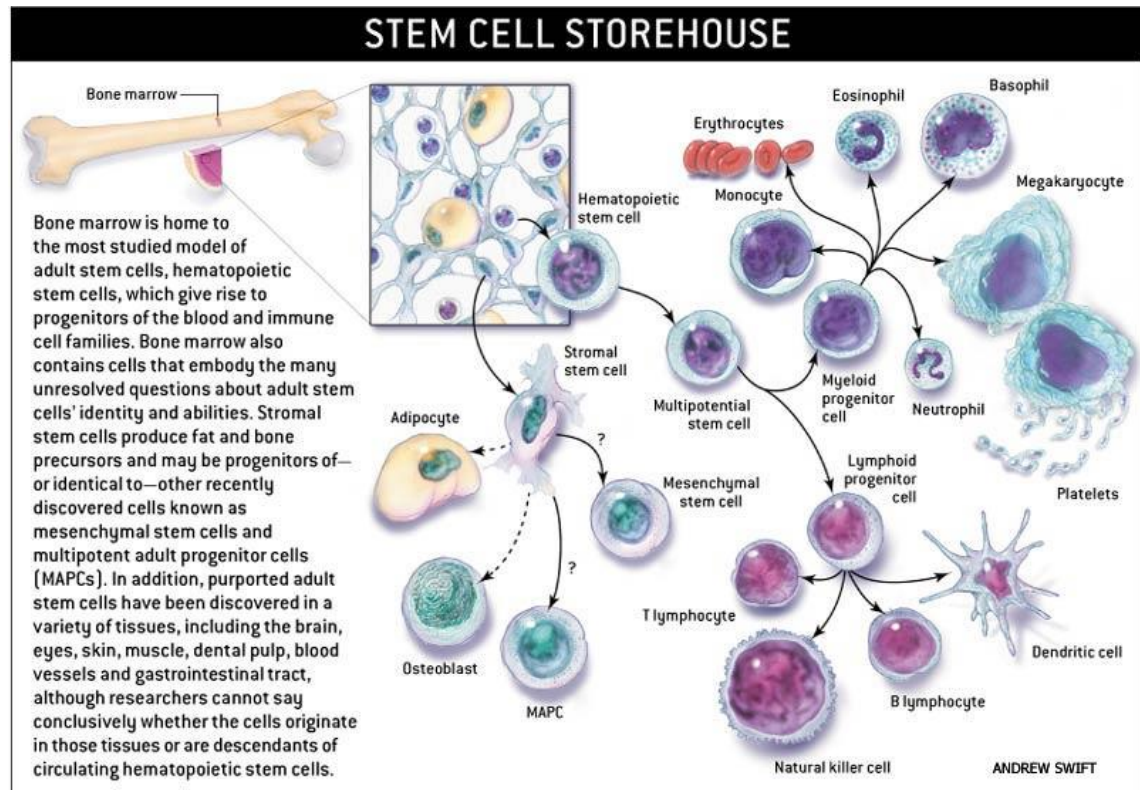
# Adult Stem Cells

Bone marrow, adipose, cord blood, placenta, etc.

Bone marrow produces several different types of stem cells

Hematopoietic stem cell (HSC)

Mesenchymal derived stromal cells (MSC)



Lanza and Rosenthal Scientific American June 2004

# Hematopoietic Stem Cells

Bone marrow, circulating adult blood, umbilical cord blood

Replenish bone marrow damaged  
by cancer treatments

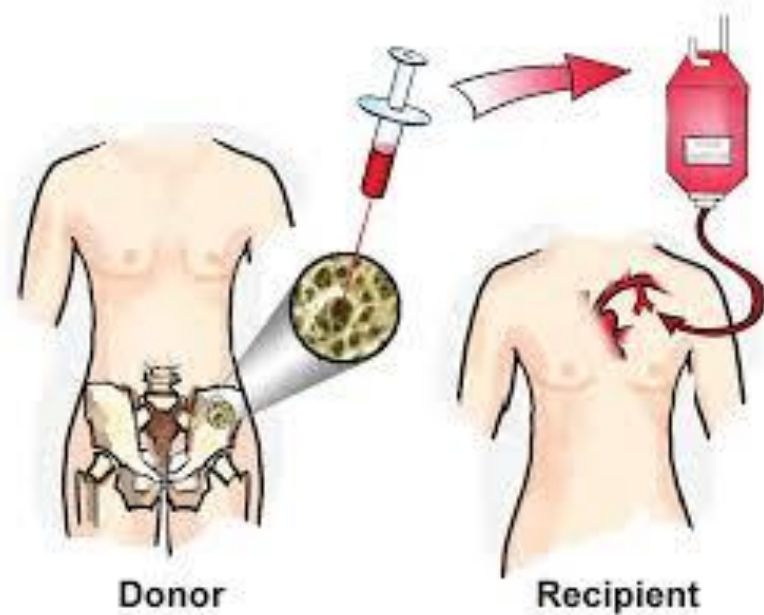
Not directly treating cancers

FDA approved for leukemias and  
lymphomas

Autologous

Allogeneic

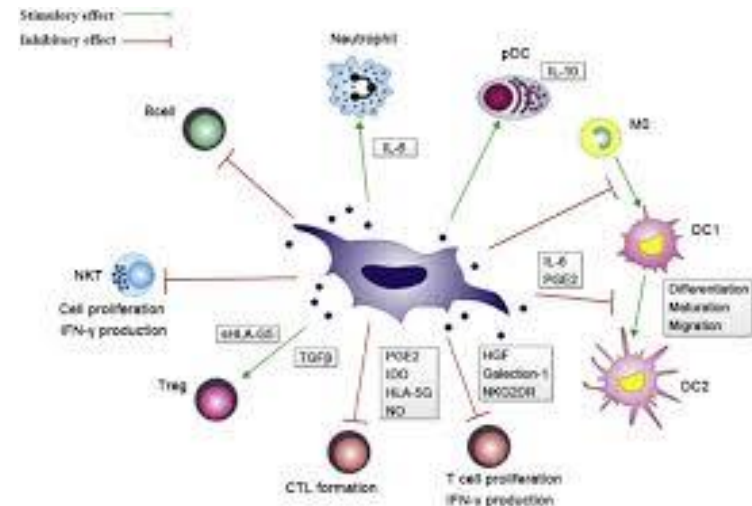
Widely and successfully utilized





# Immunomodulation: Mesenchymal Stem (Stromal) Cells

- Initially isolated from bone marrow: fat, placenta, cord blood
  - Do not circulate in adult blood
- Differentiation ability: bone, fat, cartilage
- Immunomodulatory role
  - Sample and react to inflammatory environments
- Immunoprivileged
- Many clinical trials
- Approved for limited indications in Canada, New Zealand, India, and South Korea



**No FDA-approved use in US**

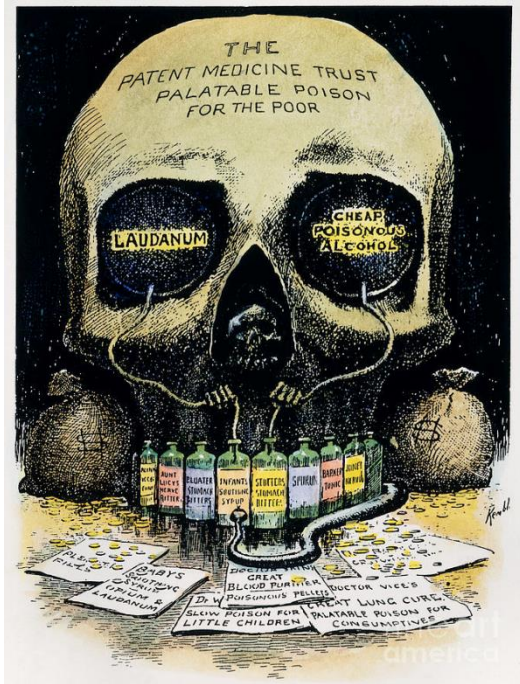
**Nothing on-label: no justifiable “off-label” uses**

# Unproven “Stem Cell” Therapies

- Research and clinical realities:
  - Few cell-based therapies are standard-of-care or approved by regulatory agencies
- Patient expectations:
  - Patients with chronic or end-stage diseases will seek unproven (stem) cell treatments motivated by therapeutic hope
  - High global demand for (stem) cell-based therapies
- The (problematic) answer:
  - Worldwide proliferation of “stem cell” clinics
  - Unproven, untested and potentially dangerous (stem) cell treatments
  - Different regulatory frameworks exacerbate the problem



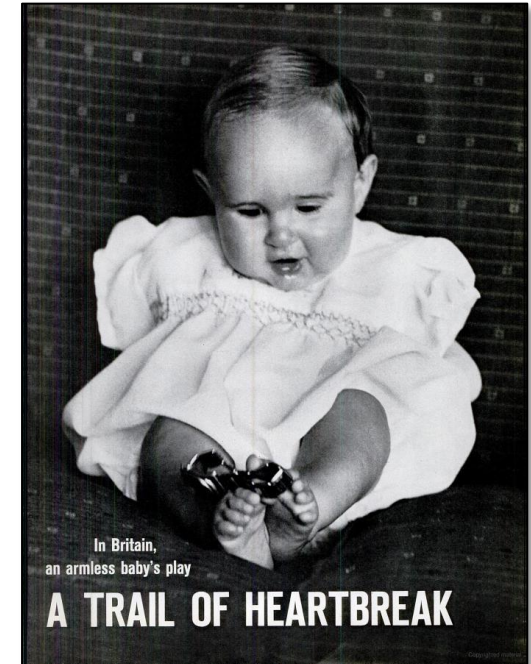
# History of US drug regulation



1906 – US FDA established;  
accurate **labeling**

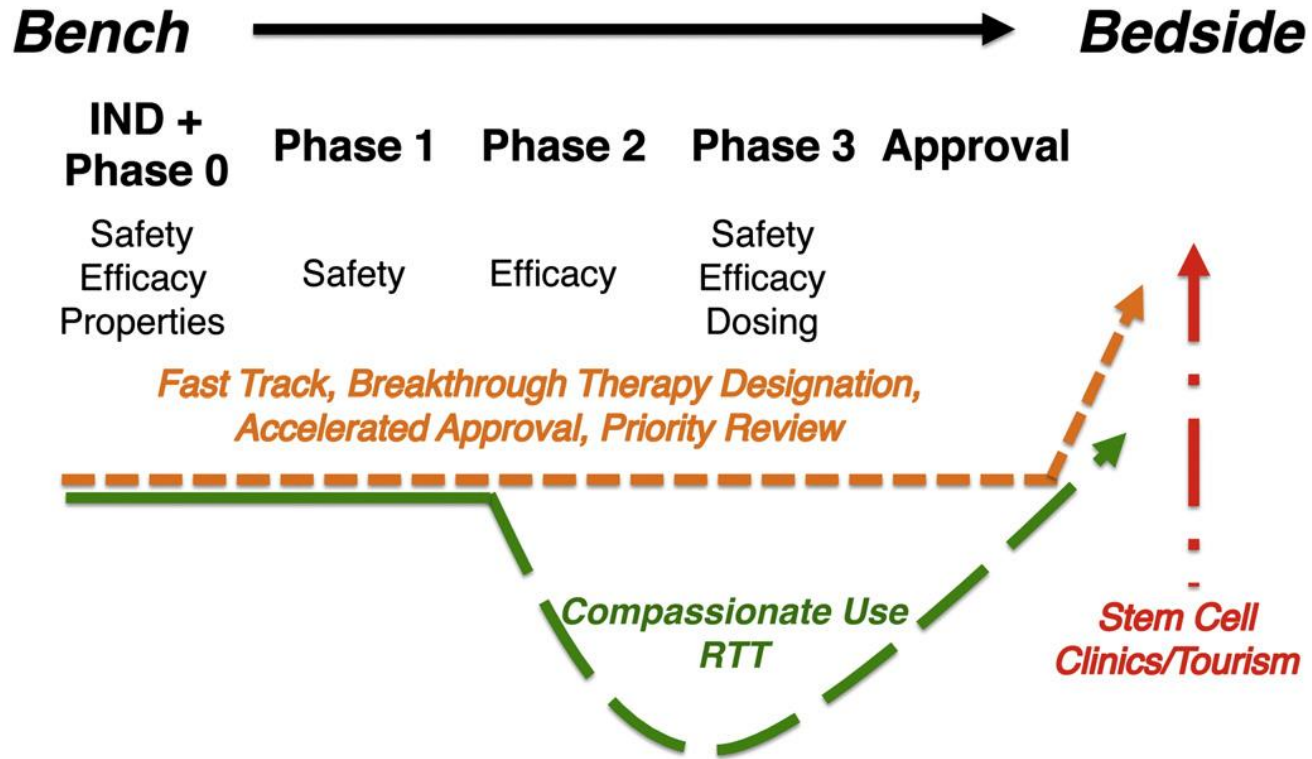


1938 – Passage of Food, Drug, and Cosmetic Act (FDCA); **safety** testing



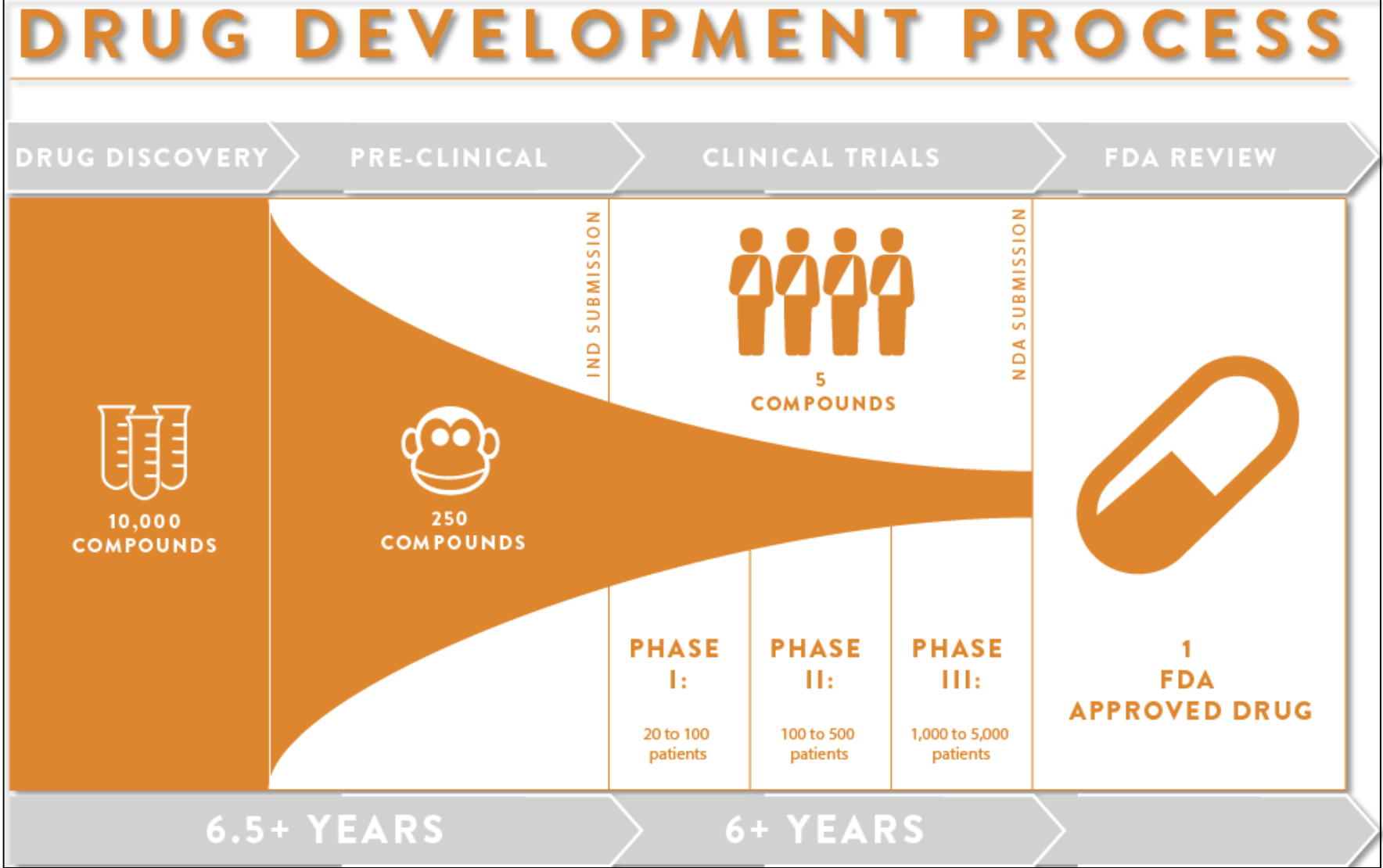
1962 – FDCA amended to require **efficacy** testing  
\*(PMDA established in 2000)

# FDA Pathways for New Therapies



Knoepfler, Adv Drug Deliv Rev, 2015

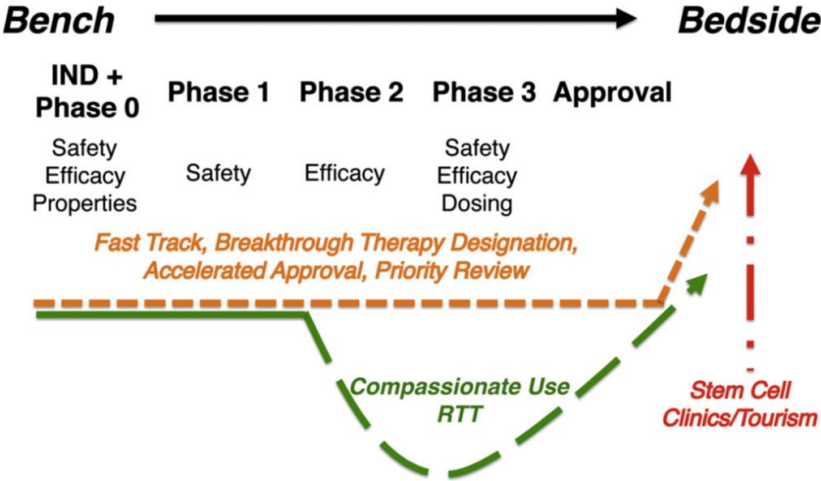
# FDA Pathways for New Therapies



# Speeding the Process

## Regenerative Medicine Advanced Therapy (RMAT)

- Cell therapy intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and has the potential to address unmet medical needs for such disease/condition
- Preliminary clinical evidence
- Use of real world evidence (e.g. observational data)



# Speeding the Process

As of December 31, 2020:

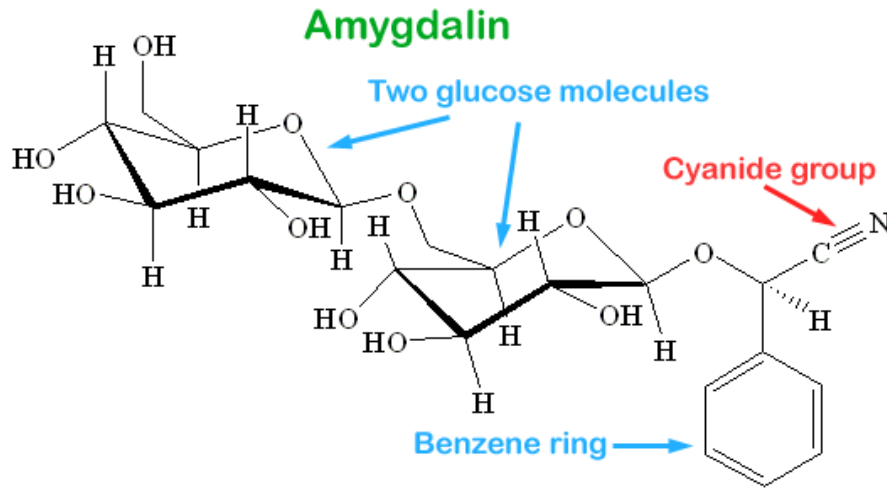
- 155 Regenerative Medicine Advanced Therapy (RMAT) designation requests received overall
- 59 RMAT requests granted overall
- 1 product has received marketing authorization (Breyanzi (lisocabtagene maraleucel))
- Indications vary widely – stroke, spinal cord injury, sickle cell disease, muscular dystrophy, others
- Major benefit: accelerate regulatory approval process



# Medical Tourism

Travel to a country with less stringent regulations

Obtain treatment not otherwise available





# Stem Cell Medical Tourism



COUNTRY	% OF CLINICS
1. USA	27
2. China	12
3. India	12
4. Thailand	11
5. Mexico	9
6. Argentina	3
7. Australia	3
8. Austria	3
9. Germany	3
10. Ukraine	3
11. Malaysia	3
12. Colombia	1
13. Dominican Republic	1
14. Israel	1
15. Korea	1
16. Lebanon	1
17. New Zealand	1
18. Panama	1
19. Phillipines	1
20. Russia	1
21. Spain	1

- An estimated 60,000 patients treated every year with unproven stem cell therapies
- Between \$300 million and \$2.4 billion spent every year on such treatments

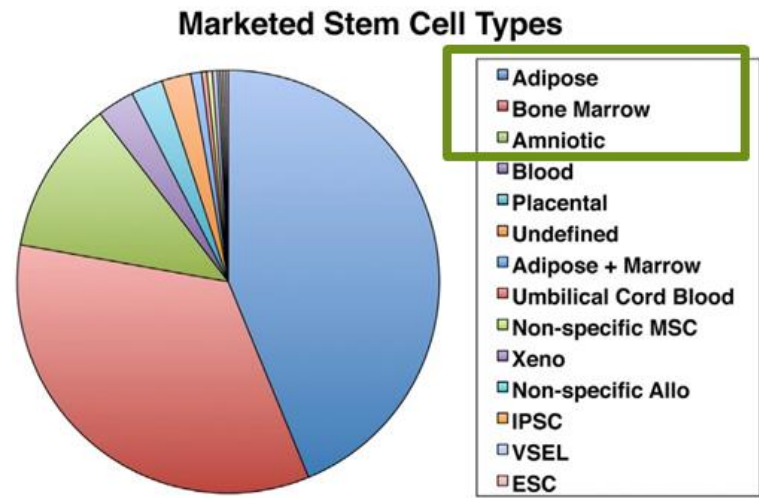
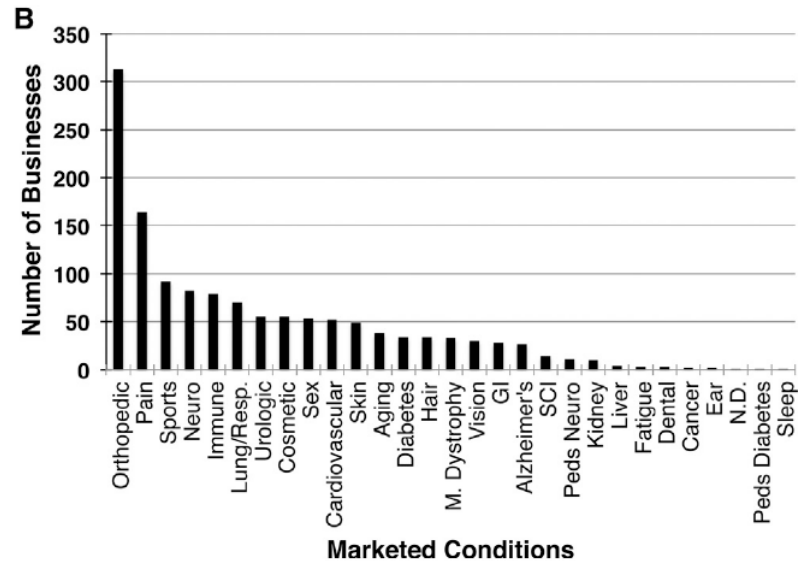
Connolly et al., Travel Med. Infect. Dis., 2014

Deans et al., Cytotherapy, 2016

# Defining Unproven Cell-Based Therapies

- Unclear scientific rationale to suggest efficacy
- Lack of understanding of scientific mechanism and/or biologic function to support clinical use
- Insufficient data from laboratory studies, animal models, or clinical studies to support use in patients
- Lack of a standardized approach to confirm product quality or manufacturing consistency
- Inadequate information disclosed to patients in order to obtain proper informed consent
- Use of non-standardized or non-validated methods of administration
- Uncontrolled experimental procedures in humans

# Unproven Stem Cell Interventions



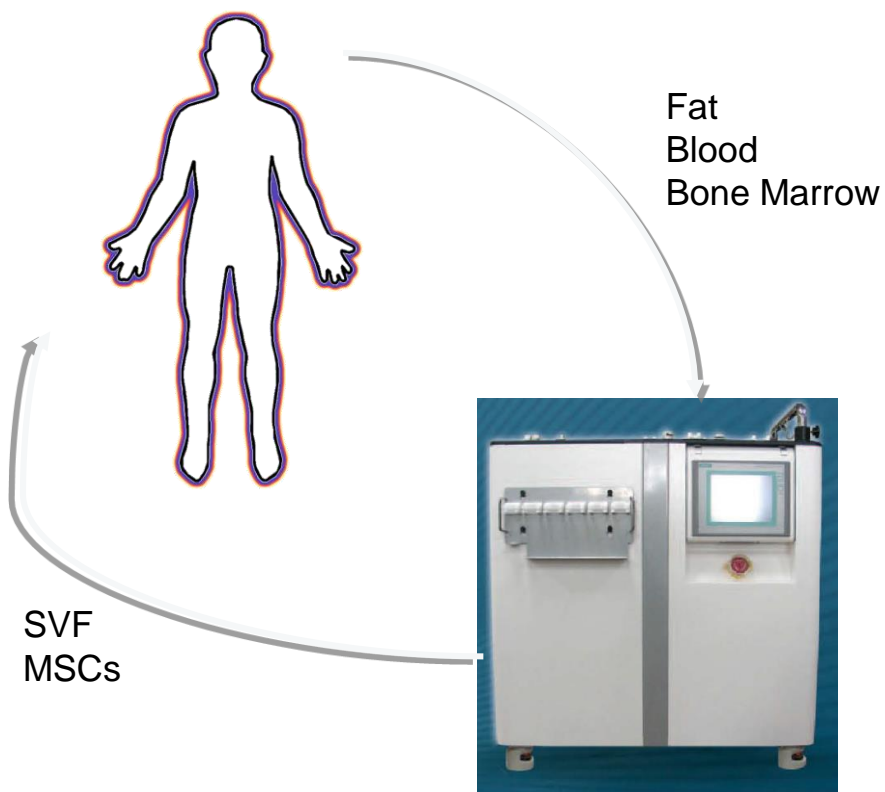
- Mode of administration:
  - Intravenous
  - Intrathecal
  - Intramuscular
  - Nebulized

Turner and Knoepfler  
Cell Stem Cell 2016

# Stem Cell Clinics and FDA Regulations

- Human cells and tissue-based products (HCT/Ps) are considered drugs (section 351 of the PHS Act): need demonstration of safety and efficacy (e.g. through clinical trials)
- Exceptions to this rule:
  - Cell products that are **minimally manipulated**, intended for **homologous use** and not combined with other articles (section 361 of the PHS Act)
  - Destined for use in the same individual within the same surgical procedure (surgical exemption)
- Most stem cell businesses in the US claim these two exemptions to avoid having their products/interventions considered as drugs

# Unproven Stem Cell Interventions



Same day collection, isolation and re-administration

Turner and Knoepfler,  
Cell Stem Cell, 2016

# Stem Cell Clinics: Target Aging Demographics



Turner and Knoepfler 2016

# Businesses offering unproven stem cell interventions

## Misleading advertisement

- Direct-to-consumer advertising
  - Social media
- Registration to [clinicaltrials.gov](https://clinicaltrials.gov)



# Businesses offering unproven stem cell interventions

## Misrepresentation of risks and benefits

- Portrayal of treatments as routine (instead of experimental and unproven)
- Exaggerated claims of safety and efficacy
- Absence of quantitative outcomes and/or poor patient follow-up



# Businesses offering unproven stem cell interventions

## Patient targeting

- Patient seminars (essentially sales pitch)
- Pressure on prospective patients to take on debt or crowdfund

## Not covered by insurance

The image shows a newspaper clipping from The Washington Post. The main headline is "Clinic makes its pitch: Beg, borrow and heal". The sub-headline reads "Lung Health Institute offers unproven treatments to desperate patients — and even coaches them on raising the cash". The article is by William Wan and Laurie McGonley. It features a photograph of a woman, Tamey Rivers, who is seeking class action status in a lawsuit against the Lung Health Institute. The article discusses how the clinic targets desperate patients, often coaching them to raise money through crowdfunding or by selling assets like their homes. It also mentions that the clinic's treatments are unproven and that the institute has been criticized for aggressive marketing. A sidebar on the right of the clipping has a headline "Ukraine leader in risky position" and a sub-headline "CORRUPTION FIGHT MAY ANGER TRUMP".

**The Washington Post**  
MONDAY, DECEMBER 2, 2019 • \$2

### Clinic makes its pitch: Beg, borrow and heal

Lung Health Institute offers unproven treatments to desperate patients — and even coaches them on raising the cash

BY WILLIAM WAN AND LAURIE MCGONLEY

By the time he called the Lung Health Institute, Ed Garbett was desperate. The Dallas computer parts salesman could barely walk the length of his house without gasping for breath. Unable to work, Garbett, 44, was going broke paying for trips to the emergency room.

Lung Health Institute staffers were recruiting. Garbett recalled, telling him that more than 90 percent of their patients with lung disease said they found relief through their stem cell treatments — which would cost him \$5,000, thanks to a seminar sale. He said they told him that if he didn't have the money, he could get it other ways, like refinancing on GoFundMe.

So Garbett raised \$1,000 in donations, tapped the last of his savings and charged the rest on his credit card. "I spent every dime I had," he said, "hoping it would make a difference."

Over the past decade, hundreds of clinics have sprouted across the United States selling stem cell therapies for incurable conditions like Garbett's lung disease, Parkinson's disease and muscular degeneration. But often, patients see the only thing allowed in their features.

Former patients of the Tampa-based Lung Health Institute said they were encouraged to take out bank loans or borrow money from family members. Some withdrew from their retirement accounts and took up church offerings. Others borrowed against their homes.

"What they're doing is taking a predatory approach to people with progressive, fatal diseases," said Gregory Coopers, chief medical officer for the Pulmonary Fibrosis Foundation. His foundation issued a warning this year against such stem cell therapies, noting that desperate patients continue to "succumb to an onslaught of marketing and branding."

Even in a booming industry long denounced by medical experts, the Lung Health Institute has been singled out for its aggressive marketing and

**HEALTHCARE SCANDAL**

**Ukraine leader in risky position**  
CORRUPTION FIGHT MAY ANGER TRUMP  
Giuliani contact is ousted in review of prosecutors

BY MICHAEL BERNBAUM AND DAVID L. STERN

KYIV, UKRAINE — By the end of

Photo by AP/Wide World via Getty Images

Check, p. 42 | 36 • Tomorrow: Monday, Dec. 23/17 | 26

Democracy Dies in Darkness

MONDAY, DECEMBER 2, 2019 • \$2

PHOTO: MICHAEL O'NEILL/GETTY IMAGES

MILOŠ I. MILANOVIĆ/REUTERS/GETTY IMAGES

Tamey Rivers said in a lawsuit against the Lung Health Institute of deceptive marketing.

# An unproven/unauthorized use of cell therapy disaster

*The* NEW ENGLAND JOURNAL *of* MEDICINE

BRIEF REPORT

Vision Loss after Intravitreal Injection  
of Autologous “Stem Cells” for AMD

# Unproven/unauthorized use of cell therapy

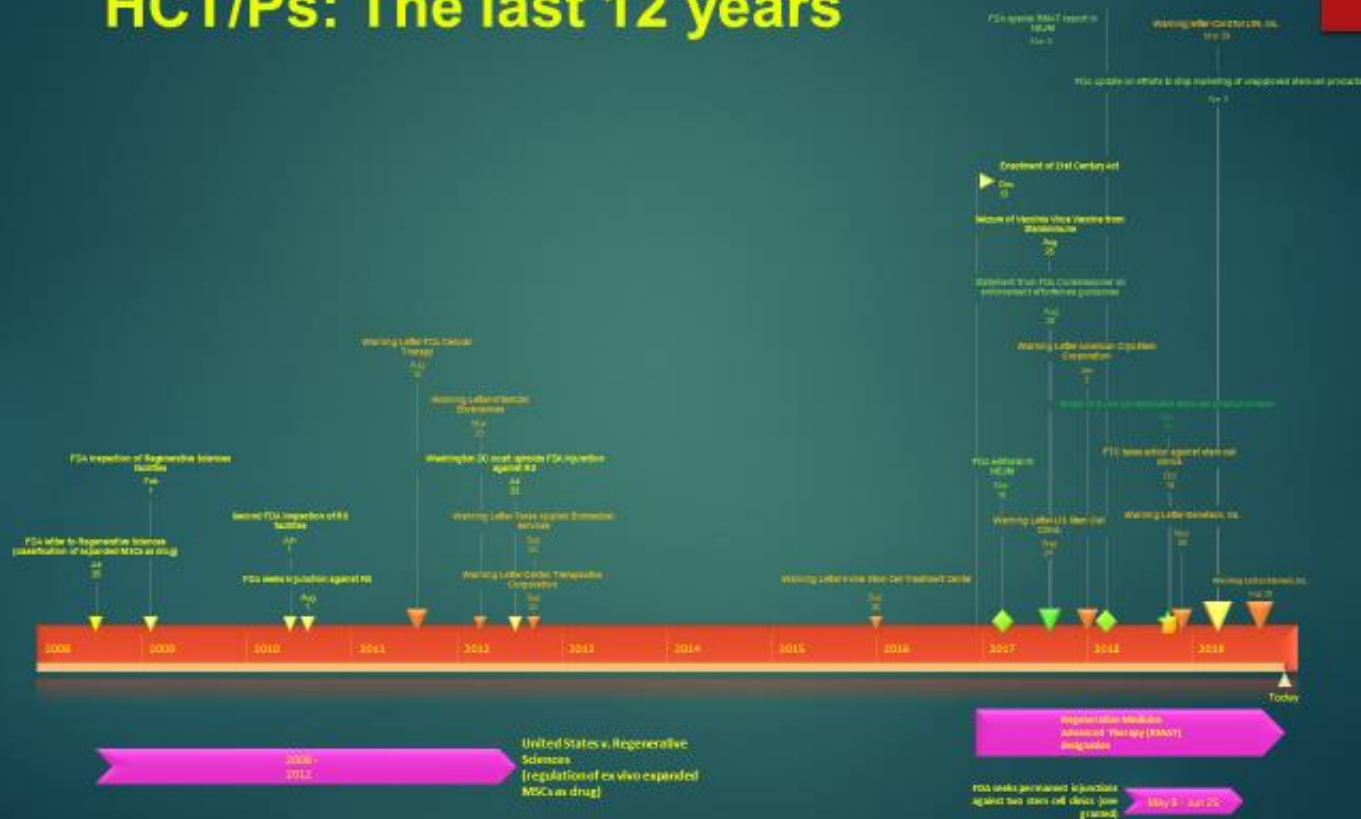
Missouri state lawmaker charged with selling fake stem cell treatments and claiming they are a cure for Covid-19



# Fighting Back

## U.S. F.D.A. Regulatory Action on HCT/Ps: The last 10 years

### US FDA Regulatory Action on HCT/Ps: The last 12 years



# Fighting Back

## Increasingly negative public perceptions of unproven "stem cell" interventions

### Highly publicized cases of patients harmed by unproven cell-based interventions

**VISION EXPERT**

Vision Loss after Intravitreal Injection of Autologous "Stem Cells" for AMD

Glioproliferative Lesion of the Spinal Cord as a Complication of "Stem-Cell Tourism"

N ENGL J MED 375:2 NEJM.ORG JULY 14, 2016

### Negative coverage by lay press

**Sun Sentinel**

A deeper look at stem cell clinic where 3 patients lost sight after treatment

**Tampa Bay Times**

Unsatisfied former patient files class-action lawsuit against Lung Institute

**Los Angeles Times**

The stem cell therapies offered by this La Jolla clinic aren't FDA approved, may not work — and cost \$15,000

**The Washington Post**

Miracle cures or modern quackery? Stem cell clinics multiply, with heartbreaking results for some patients.

**CR** Consumer Reports

**The Trouble With Stem Cell Therapy**

A new industry is booming. But critics worry that the treatments are ineffective and dangerous. Here's how to protect yourself.

**The New York Times**

*F.D.A. Moves to Stop Rogue Clinics From Using Unapproved Stem Cell Therapies*

FIRST OPINION

# Kudos to Google for banning stem cell ads. Other tech companies should follow

By JEREMY SNYDER / SEPTEMBER 24, 2019



DENIS CHARLET/AFP/GETTY IMAGES

**G**oogle took an important step this month toward restricting the reach of one breed of 21st-century snake oil purveyor: those selling stem cell treatments. Others need to follow its lead.

[More than 600 clinics](#) in the U.S. and [many more](#) around the world have co-opted the *potential* of using stem cell treatments to cure a range of medical conditions and now sell these treatments

## Fighting Back

# VERMONT MEDICAL SOCIETY RESOLUTION

## Stem Cell Clinics

- **RESOLVED**, that the Vermont Medical Society disseminate evidence-based information to its members regarding stem cell clinics and therapies and encourage members to have evidence based discussions with their patients when they inquire about such services; and be it further
- **RESOLVED**, that VMS coordinate with appropriate professional licensing boards, the Attorney General's Office and other regulatory bodies to ensure that patients seeking stem cell therapies are provided safe and evidence-based information and services.

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