HYPE, HEALING & HOAXES

A BALANCED LOOK AT STEM CELL THERAPY IN THE CARIBBEAN

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CONTEXT & BACKGROUND

WHAT ARE STEM CELLS AND WHAT IS STEM CELL THERAPY?

Stem cells are unspecialized cells in the body that can (a) differentiate into specialized cells and (b) self-renew rapidly. Embryonic stem cells (ESCs), present in the early stages of life are extremely potent – they can become any cell in the adult body. However, use of these has largely stalled since it involves the destruction of an embryo.

There are also adult stem cells, present throughout life, such as hematopoietic stem cells (HSCs) which are present in the bone marrow and can become different types of blood cells. Bone marrow transplants to replace HSCs are now widely recognized as a treatment.

This report will focus on another kind of adult stem cell...

Mesenchymal stem cells (MSCs) are the major players in stem cell therapy; yet they are not, in fact, stem cells! Mesenchymal stem cells were named in 1991 when Caplan et al. showed that cells from bone marrow could be induced with chemicals to differentiate into cells that make up fat, bone, and connective tissue. From the start, however, these stem cells never showed any differentiation once injected back into the body – they did not regenerate tissue by becoming that tissue. Instead, MSCs exerted a healing effect by their ability to migrate to injury sites and to signal to other cells to come and fix things (paracrine effect). In 2017 Caplan himself called for a name change, but thus far MSCs are still called...MSCs.

The initial hype of a 'stem cell' that could be obtained so easily ignited waves of **mesenchymal stem cell therapy** (MSCT) – harvesting your own cells, or those of a donor, and re-injecting them into your body. This was criticized by many as premature commercialization as there was so much unknown about these cells. While there do exist MSC treatments approved by major agencies, such as those of Canada and South Korea, the FDA – the gold standard for regulation – has issued stern warnings against it.

CONTEXT & BACKGROUND

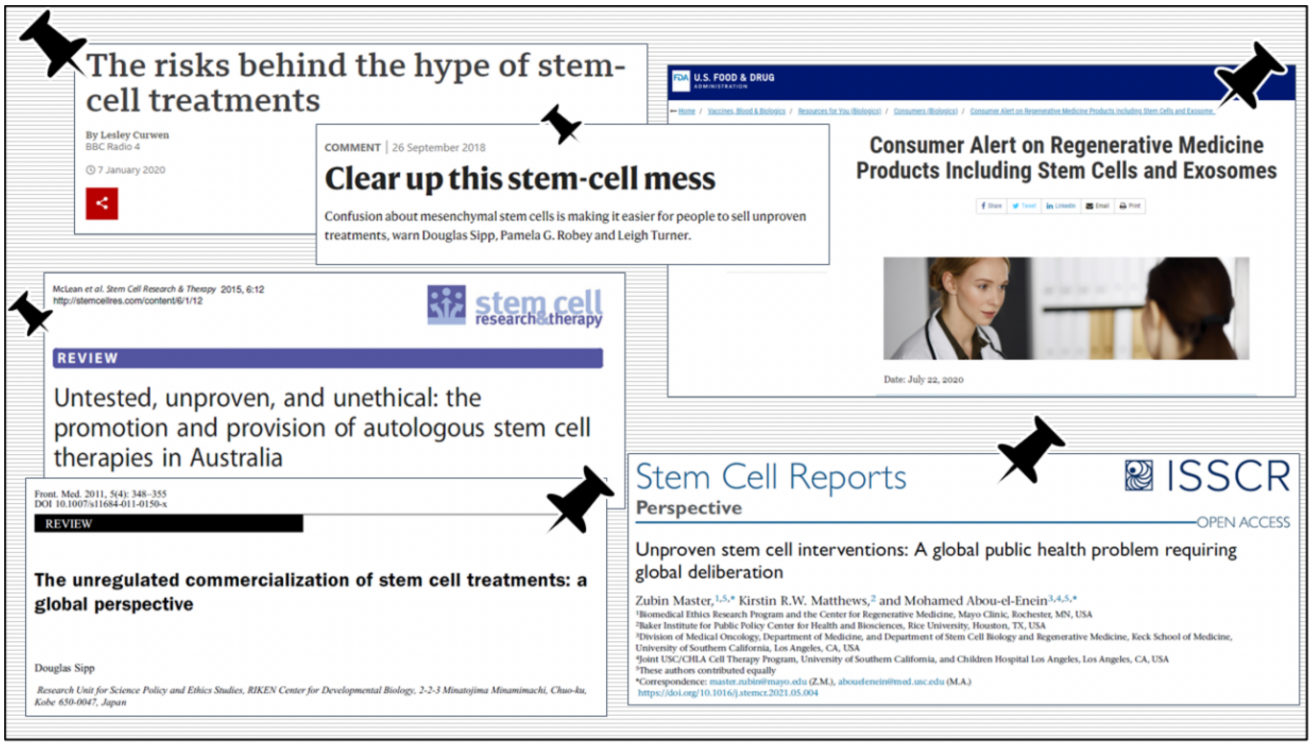

Figure 1: Snapshots of news articles, scientific reviews, and government body briefings on the dangers of unproven stem cell therapy

Despite a severe lack of evidence to support efficacy, the MSCT industry continues to boom as clinics worldwide offer unregulated therapy in response to high levels of customer/patient 'faith' and demand.

Does all this negative press and lack of supporting evidence mean all is lost? No. Don't throw out the baby with the bathwater. The presence of fraudulent clinics does not imply the absence of respectable ones.

NuMed, a clinic in T&T, has argued that "big pharma doesn't like it". And there may be validity to this. Autologous stem cell therapy uses your own cells – removing the requirement for centralized manufacturing and prevents monopolizing of the market. DVC Stem in the Cayman Islands argues that the regulatory procedures are too bogged down in bureaucracy to flex with the rapidly changing field of regenerative medicine, again a valid point, as new pharmaceutical drugs can take around 10 years and cost many millions to bring to market.

SAFETY & EFFICACY

Disease	Safe	Efficacious	# of CT(s)	Year Published
Spinal Cord Injury	Yes	Variable	38	2020
Multiple Sclerosis	Yes	No	5*	2019
Osteoarthritis	Yes	Variable	18	2021
Rheumatoid Arthritis	Yes	Variable	9	2020
COPD	Yes	No	14	2021

Table 1: Safety and Efficacy of Stem Cell Therapy based on recent reviews of clinical trials for various conditions. *Not a review – conglomerate of clinical trials

So, what does the FDA need for approval? On the surface it's a demonstration of safety and efficacy (the treatment working reliably).

All reviews concluded that MSCT was safe. Supporting this, a 2012 report reviewed 36 clinical trials and found no adverse effects, including cancer formation, and a 2018 report specifically scouting for serious adverse effects found 35, all of which related to absurd clinical decisions/errors (e.g., using animal cells instead of human ones). This suggests that MSCT is safe, once conducted in a sensible manner.

However, when it comes to efficacy, there is still a significant gap between preclinical (with animals) and clinical success. For example, in the rheumatoid arthritis case, nearly 100 preclinical studies showed that MSC therapy significantly reduced arthritis progression, yet clinical results were underwhelming. In trials with 'variable' efficacy there were cases of remarkable recovery, but this was often transient, and the results varied greatly. For multiple sclerosis and COPD there was no significant improvement. Without fail, each review called for further testing, to reliably determine efficacy.

> ***"Patients should be aware of the poor clinical results obtained thus far in clinical trials to prevent exaggerated expectations."***
>
> 2019 MSCs for Spinal Cord Injury Review

CARIBBEAN LANDSCAPE

The Caribbean and Latin America are ideal targets for endeavoring stem cell clinics because of their proximity to the U.S. and lack of stringent regulation.

CARIBBEAN LANDSCAPE

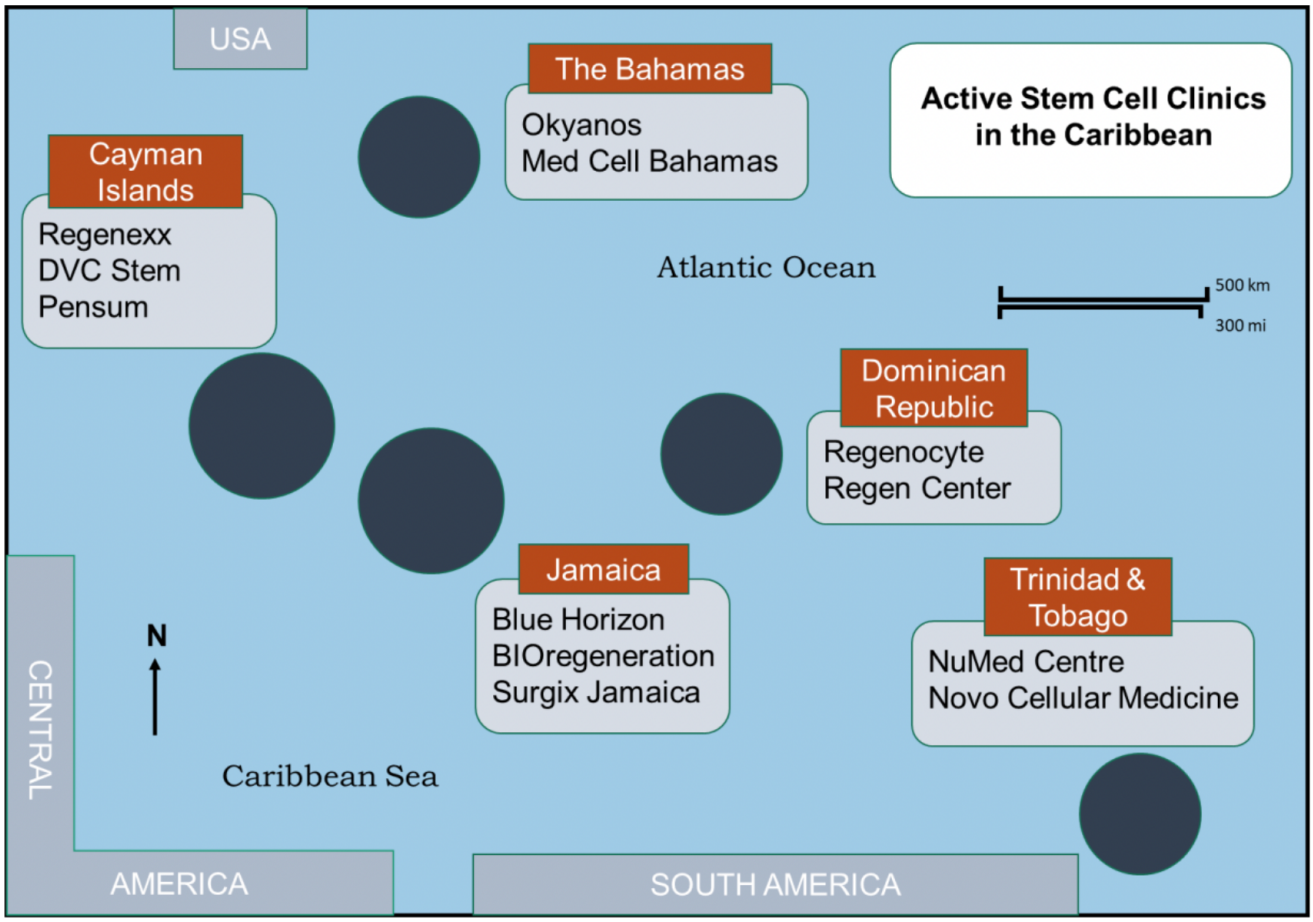

Figure 2: Active Stem Cell Clinics in the Caribbean as of July 2021, with an online presence.

Regulatory Status: According to the Food and Drugs Act of Trinidad and Tobago (T&T), a 'drug' includes any substance sold or represented for use in the treatment of a disease or disorder; further, any drug on the market in T&T must be approved by the Food & Drug Advisory. No cell therapy is approved for use in T&T. This may also be the case in the Dominican Republic and Jamaica. The nation of Antigua & Barbuda passed a 'Stem Cell Research and Therapy Act' in 2019, but that seems to be the extent of the government's involvement. However, in the Cayman Islands and the Bahamas there seem to be some regulations in place. The Bahamas has a Stem Cell Ethics Committee which oversees all stem cell therapy (SCT) in the country, and the facilities in Cayman Islands are reportedly 'fully licensed and inspected by the

government', which, as a British Overseas Territory, may carry a reasonable amount of weight. (Granted, Britain has its own unregulated stem cell therapy issues).

Doctors: I spoke with three prominent doctors within the T&T public health system. None of them was aware of stem cell clinics in Trinidad, and they had only heard of stem cell therapy vaguely. They confirmed that while the practice was likely to be illegal officially, in practice the lack of regulatory approval was unlikely to make a difference.

Insurance: Another factor that carries great weight in the advance of SCT is the stance of insurance companies – if they were to cover the therapy, it would lend massive credibility to its efficacy, as well as increase its accessibility. In this regard also, the Cayman Islands seems to be paving the way, with insurance companies covering stem cell treatments for locals.

I spoke with a senior official at Guardian Life Trinidad who confirmed that experimental therapies – those without widespread medical approval – are not covered by policy. Guardian Life was aware of a stem cell clinic operating in Trinidad but point-blank rejected any related claims.

EVERYTHING IS NOT WHAT IT SEEMS

A 2017 report featured a list of 'co-opted tokens of scientific legitimacy' which stem cell clinics use to give the impression that the clinic is scientifically sound; an adapted version is presented below. Many of these tokens were present in Caribbean clinics.

A good case in point is Regenocyte, a clinic in the Dominican Republic. On the surface, it features numerous testimonials but the website does not show that their chief doctor, Zannos Grekos, had his license revoked by the State of Florida after two of his SCT patients died. This is not to say that the testimonials are necessarily not true, but certainly, there is more than what meets the eye.

Another case study is Novo Cellular Medicine Institute in Trinidad.

EVERYTHING IS NOT WHAT IT SEEMS

Co-opted Tokens of Scientific Legitimacy	
Accreditations and awards	Claiming accreditation of products or international training
Boards and advisors	Featuring boards with highly accoladed academics/medics
Clinical study registration	Registering trials without any real scientific backing
Ethics review	Simply using this term without evidence
Location	Renting of space withing legitimate institutions
Membership	Joining established academic or professional societies
Outcome registries	Relying on voluntary, self-reporting registries instead of controlled clinical trials
Patenting	Advertising patent applications (that have not even been approved)
Publication	Publishing results in [often sub-standard] journals
Rationales	Citing preclinical data and 'promising' results
Self-regulation	Forming organisations to self-regulate
Technical language	Using scientific-sounding words
Testimonials and endorsements	Judiciously selecting favorable testimonials, or using celebrity comments

Figure 3: Co-opted Tokens of Scientific Legitimacy, adapted from Sipp et al., 2017.

They advertise all their procedures as being part of 'clinical trials,' but only two were ever registered on ClinicalTrials.gov; neither one is completed. This is not to say that this particular clinic is misleading per se, but rather it highlights the unreliability of superficial claims.

> ***"It can be difficult even for professionals, let alone patients, to determine whether these tokens demonstrate true compliance with the standards."***
>
> Sipp et al., 2017

CONCLUSION

Efficacy – Proof of large-scale efficacy seems to be lacking for every application of SCT, so one may be paying for a life-changing therapy, but instead only receive transient pain-relief.

Uniformity – The lack of regulation means that one clinic's standards are not another's, leaving it to patients to make decisions without enough information.

Insurance – Costs are still quite high, and many insurance companies will not cover experimental treatments, thus limiting accessibility.

CONCLUSION

Greed – The human factor of greed cannot be ignored and is likely the driving force behind harmful profiteering.

'Inertia' – For any new treatment, there is a degree of resistance, and this is amplified by capitalism and/or bureaucracy. There is also a great degree of inefficiency in small island governments, which can hinder innovation. This lends some weight to the idea of using a treatment before full traditional regulation has approved it.

Easy – The MSCT procedure is relatively non-invasive, usually involving a bone marrow aspirate or liposuction, and there is little-to-no recovery time.

Safety – The safety of MSC therapy has consistently been shown through clinical trials and other reports.

Life-changing – There seems to be evidence that for some people the treatment has made a significant life impact. Given the right-to-try principle, and safety of the procedure, this is precedent for allowing the therapy, once patients are well informed.

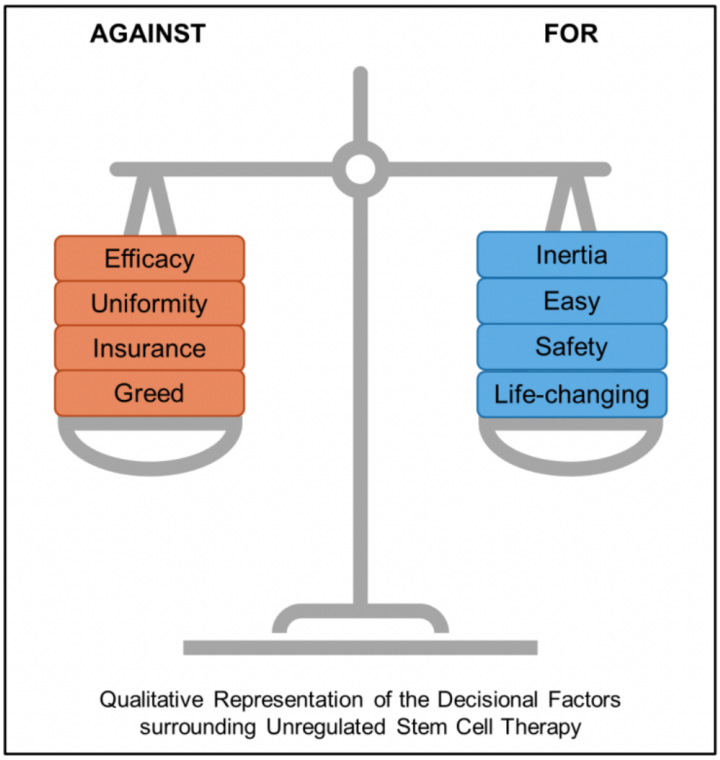

Figure 4: A Balanced look at unregulated stem cell therapy.

Given a reputable clinic, stem cell therapy may prove over time to be a viable option, especially if other methods tried by patients have been fruitless. With continuing research and regulation (such as a government-mandated Cell Therapy Clinic Accreditation Program) stem cell therapy will hopefully become more efficacious, reliable, and accessible – and hopefully will get its name changed to just 'cell therapy'!

FURTHER READING

INTERNATIONAL ORGANIZATIONS

International Society for Stem Cell Research (ISSCR)
International Society for Cell & Gene Therapy (ISCR)

CRITICISM OF UNREGULATED STEM CELL THERAPY

Marketing of unproven stem cell-based interventions: A call to action

REVIEWS OF CLINICAL TRIALS

Clinical Trials of Stem Cell Treatment for Spinal Cord Injury

MEsenchymal StEm cells for Multiple Sclerosis (MESEMS)

Meta-Analysis of Adipose Tissue Derived Cell-Based Therapy for the Treatment of Knee Osteoarthritis

Mesenchymal Stem/Stromal Cells for Rheumatoid Arthritis Treatment: An Update on Clinical Applications

Stem Cell Therapy for COPD

SAFETY

Concise Review: A Comprehensive Analysis of Reported Adverse Events in Patients Receiving Unproven Stem Cell-Based Interventions

Safety of Cell Therapy with Mesenchymal Stromal Cells (SafeCell): A Systematic Review and Meta-Analysis of Clinical Trials

CHANGE THE NAME

Mesenchymal stem cells: Time to change the name