

REVIEW

## Stem cells, regenerating medical therapeutics

### Células madre, regenerando la terapéutica médica

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#### ABSTRACT

**Introduction:** the purpose of regenerative medicine is to stimulate or regenerate cells, tissues or organs in order to restore or establish normal function. Of its procedures, stem cell therapy is undoubtedly the one that has advanced the most. Its use constitutes a novel therapeutic alternative to diseases treated by different medical specialties, not escaping from it the recent disease caused by the SARS-CoV-2 virus, COVID-19.

**Objective:** to describe the application of stem cell therapy in different medical specialties and in the treatment and rehabilitation of COVID-19 positive patients.

**Method:** a literature review was performed by consulting original articles, case reports and open access systematic reviews in peer-reviewed academic publications from the last 5 years. The databases of ScieELO, Regmed, Dialnet, Mayoclinic, among others, were reviewed. Search terms included Stem cells, Stem cell therapy, Stem cell therapy applications, as well as their translation into English.

**Development:** Stem cell therapy has given rise to what can be categorized as regenerative cell therapy, and is currently one of the most innovative topics in contemporary medicine. The applications of these cells can be divided into two groups: to regenerate destroyed tissues or as a therapeutic vehicle for genes, such applications are used for the treatment of diseases by different medical specialties.

**Conclusions:** This therapy constitutes an excellent alternative for the treatment and rehabilitation of multiple diseases treated by different medical specialties, among them the current COVID-19.

**Keywords:** Regenerative Medicine; Stem Cell Therapy; Applications; Therapeutic Alternative; Diseases; Medical Specialties; COVID-19.

#### RESUMEN

**Introducción:** la medicina regenerativa tiene como propósito estimular o regenerar células, tejidos u órganos con la finalidad de restaurar o establecer una función normal. De sus procedimientos, sin duda alguna, el que más ha avanzado, es la terapia de células madre. Su empleo constituye una novedosa alternativa terapéutica a enfermedades atendidas por las disímiles especialidades médicas, no escapando de ello la reciente enfermedad provocada por el virus SARS-CoV-2, COVID-19.

**Objetivo:** describir la aplicación de la terapia de células madre en las diferentes especialidades médicas y en el tratamiento y rehabilitación de pacientes positivos a la COVID-19.

**Método:** se realizó una revisión bibliográfica consultando artículos originales, reportes de caso y revisiones sistemáticas de acceso abierto en publicaciones académicas revisadas por pares, de los últimos 5 años. Se revisaron las bases de dato de ScieELO, Regmed, Dialnet, Mayoclinic, entre otras. Los términos de búsqueda incluyeron Células madre, Terapia de Células madre, aplicaciones de la terapia de células madre, así como

su traducción al inglés.

**Desarrollo:** el tratamiento con células madre ha dado lugar a lo que se puede catalogar como terapia celular regenerativa, y constituye en la actualidad uno de los temas más innovadores de la medicina contemporánea. Las aplicaciones de estas las podemos dividir en dos grupos: para regenerar tejidos destruidos o como vehículo terapéutico de genes, tales aplicaciones son empleadas para el tratamiento de enfermedades por las diferentes especialidades médicas.

**Conclusiones.** esta terapia constituye una alternativa excelente al tratamiento y rehabilitación de múltiples enfermedades atendidas por diferentes especialidades médicas, entre ellas la actual COVID-19.

**Palabras clave:** Medicina Regenerativa; Terapia de Células Madre; Aplicaciones; Alternativa Terapéutica; Enfermedades; Especialidades Médicas; COVID-19.

## INTRODUCTION

Although the term “regenerative medicine” is relatively new, the first scientific writing to mention regeneration is Aristotle’s “On the Generation of Animals”.<sup>(1)</sup>

Cohnheim’s hypothesis (1967) is the first straightforward approach to cell therapy, which is today’s most active and promising field in regenerative medicine. The work of Kleinsmith and Pierce in the 1960s describing pluripotency, the isolation of an embryonic animal cell capable of generating any tissue by Martin, Evans, and Kaufman in 1981, and finally, the isolation and culture of the first human embryonic cell by Thomson in 1998 ushered in a new era of knowledge in cell therapy. During the same period, Friedenstein’s studies on adult stem cells contained in bone marrow led to the introduction of cell therapies without ethical implications or immune rejection.<sup>(1)</sup>

Thanks to the intensive work of different biomedical groups worldwide, “regenerative medicine” began to be popularized at the beginning of the 21st century as a specific area of medical knowledge.<sup>(1)</sup>

The field of regenerative medicine is proving to be very promising, and several countries worldwide are focusing on research into this new type of treatment.<sup>(2)</sup>

Despite the damage caused by the sustained and systematic economic, commercial, and financial blockade imposed by the United States against Cuba, our country’s National Health System, thanks to the political and technical will that sustains it, has managed to create the conditions for the development of regenerative medicine. This is motivated by these new therapies’ benefits in alleviating patients’ ailments, often with results superior to conventional treatments.<sup>(3)</sup>

Regenerative medicine aims to stimulate or regenerate cells, tissues, or organs to restore or establish normal function. It is not limited to the use of stem cells but also includes the therapeutic application of various stimulating factors and other soluble elements involved in various biological processes, gene therapy, and tissue engineering, both in vitro and in vivo. Of all these procedures, the one that has undoubtedly advanced the most in a short time is stem cell therapy.<sup>(4)</sup>

The development of this therapy is a priority for several countries worldwide, with promising results being obtained in the field. In Cuba, since February 2004, when clinical research with adult stem cells began, regenerative medicine has shown extensive and admirable work in favor of one of the most significant challenges for biomedical research in the 21st century. Cuban researchers’ essential results in this medical branch have placed us alongside the most advanced countries in this field. They show that many patients in different specialties have benefited from these procedures, reaching all 15 provinces and special municipalities.<sup>(3)</sup>

The benefits of regenerative medicine have led to notable improvements in the quality of life of thousands of patients in the country’s central region who were treated by various scientific and healthcare institutions in Villa Clara. This confirms that Cuba, as a small Caribbean country, is a leader in this branch of medicine.<sup>(5)</sup>

To date, 14 specialties use these alternatives. Among them are angiology, ophthalmology, orthopedics, cardiology, natural and traditional medicine, dermatology, and rheumatology, primarily benefiting elderly patients.<sup>(5)</sup>

Due to the results obtained by regenerative medicine in the treatment of patients with stem cells through cell therapy in various medical specialties, it was decided to conduct this literature review to describe the application of stem cell therapy in different medical specialties, as well as in the treatment and rehabilitation of patients who tested positive for COVID-19. The novelty of the topic and the lack of bibliographic treatment of it are the primary motivations. The scientific problem posed is: What is the application of stem cell therapy in different medical specialties? Twenty-eight bibliographies were consulted.

**Objective:** to describe the application of stem cell therapy in different medical specialties and the treatment and rehabilitation of COVID-19-positive patients.

## METHOD

A literature review was conducted from May 2 to 22, 2021. Original articles, case reports, and systematic reviews were reviewed in open-access, peer-reviewed academic publications from the last five years with no geographical or language restrictions. The ScieELO, Regmed, and Dialnet databases were reviewed.

The search terms included stem cells, stem cell therapy, and applications of stem cell therapy, as well as their English translations: stem cells, stem cell therapy, and applications of stem cell therapy.

## DEVELOPMENT

Stem cell treatment has given rise to what can be classified as regenerative cell therapy and is currently one of the most innovative topics in contemporary medicine.<sup>(4)</sup>

### Characteristics of stem cells

According to studies conducted by the authors in various publications, a stem cell is a cell capable of dividing indefinitely and differentiating into different types of specialized cells, not only from a morphological point of view but also functionally. In addition, they can persistently implant themselves in healthy and damaged tissues. Depending on their evolutionary state (or origin), stem cells can be classified into two main types: embryonic (ESCs) and adult or somatic (ASCs).

We also note that ESCs are isolated from the internal mass of the embryo in the blastocyst stage. These cells have two exceptional properties: unlimited capacity for proliferation in culture and pluripotency. However, the properties of this type of stem cell make them controversial, as their pluripotency makes them challenging to control in the laboratory, and even after transplantation, they can induce tumors. Furthermore, due to their origin, their manipulation and use have faced strong opposition in different countries based mainly on ethical, religious, and political considerations.

Adult or postnatal stem cells come from differentiated tissue and can give rise to a few types of specialized cells. They can be found in umbilical cord blood, bone marrow, subcutaneous adipose tissue, articular cartilage, the epidermis, the brain, dental pulp, skeletal muscle (satellite cells), the pancreas, and the heart. They are easier to handle, can be autologous, and therefore do not cause immune disorders or present ethical or legal limitations, nor have they been shown to cause cancer.<sup>(4)</sup>

Another classification applied to stem cells is based on their potential and capacity for differentiation: totipotent, pluripotent, multipotent, oligopotent, and unipotent.

### Sources of stem cells used for transplantation

Among the primary stem cells with therapeutic potential are embryonic, fetal, amniotic, umbilical cord blood, adult, mainly hematopoietic, mesenchymal, and, more recently, CMPi (adult cells modified to have the properties of MSCs).<sup>(4)</sup>

According to the studies covered by the authors, in most cases, the most studied source of stem cells is bone marrow, which is known to contain not only hematopoietic stem cells (HSCs) but also other types of cells. These include endothelial progenitor cells, mesenchymal cells, oval cells, lateral population cells, and tiny cells similar to embryonic cells (VSEL cells, from “tiny embryonic-like cells”). In practical terms, bone marrow-derived mononuclear cells (BM-MNCs) are carriers of different MSCs.

HSCs have been used for over 50 years in bone marrow transplantation and have proven effective in treating various diseases.<sup>(5)</sup>

In the early days, HSCs were almost exclusively obtained from bone marrow. Later, they were extracted from peripheral blood. HSCs are capable of contributing to angiogenesis and vasculogenesis.<sup>(6)</sup>

Our comprehensive study found that mesenchymal stem cells (MSCs) originate from the bone marrow stroma. They have a high proliferative capacity and can differentiate into various cell lineages. They represent a heterogeneous group of multipotent cells characterized by low immunogenicity and high versatility in terms of their immunomodulatory effects.

Side population cells, known in the literature by the acronym SP (side population), can give rise to specialized cells and integrate into different tissues *in vivo*, including non-hematopoietic tissues.<sup>(6)</sup>

Adult multipotent progenitor cells (MAPCs) are very small MSCs with a differentiation capacity similar to that of embryonic cells. Unlike embryonic cells, MAPCs can be obtained from autologous bone marrow, which prevents rejection reactions. Furthermore, the teratogenic potential of embryonic cells has not been observed in MAPCs.<sup>(6)</sup>

Oval cells are believed to have bipotential generative capacity, as they can transform into hepatocytes and epithelial cells of the biliary tree.<sup>(6)</sup>

The stem cells used in therapy can be:<sup>(7)</sup>

- Cells from the patient themselves (autologous transplantation, autotransplantation).
- Cells from a donor (allogeneic transplantation).

### **Mechanism of action of adult stem cells**

Several hypotheses based on existing evidence have been suggested to explain these mechanisms, including:<sup>(6)</sup>

- cell transdifferentiation,
- cell fusion,
- an autocrine/paracrine effect secondary to the release by cells of different soluble molecules or cytokines with specific actions.

Two interrelated phases can be proposed in the regenerative cell therapy process. The first consists of the direct action of the implanted cells. The autocrine, paracrine, and telecine effects of the soluble molecules released represent the second, indirect phase.

The applications of stem cells can be divided into two main groups: first, their differentiation potential would allow them to regenerate destroyed or damaged tissues, as in the case of neurodegenerative diseases, diabetes, or heart disease; second, stem cells could be used as a therapeutic vehicle for genes, as in the case of monogenic diseases.<sup>(8)</sup>

Below, we describe some potential applications of stem cells in regenerative therapy for treating various diseases, including COVID-19, by different medical specialties.

### **Clinical applications of stem cell therapy in cardiology**

Cell implantation in non-viable cardiac areas has been extensively developed in basic research with favorable results. This therapy has several objectives: to replace damaged necrotic and hyperfunctioning myocytes; to improve angiogenesis and vasculogenesis in the damaged heart; to limit the expansion of scar tissue and ventricular dilatation, which potentially increases regional contractility and improve ventricular function; and to optimize the heart's contractile function.<sup>(9)</sup>

From an experimental standpoint, several studies have already tested the use of various types of stem cells in different models of myocardial injury. Among the types of cells used are skeletal myoblasts, unpurified bone marrow cells, fetal cardiomyocytes, mesenchymal stem cells, and embryonic pluripotent cells.<sup>(10)</sup>

Numerous experimental studies have shown that the transplantation of autologous or allogeneic stem cells can improve left ventricular ejection fraction (LVEF), reduce infarct size, and prevent pathological ventricular remodeling.<sup>(9)</sup>

Tissue-engineered cardiac pacemakers (TECPs) have emerged to treat sinus node dysfunction, effectively avoiding the above problems. TECPs, as spontaneously beating tissues, can be manufactured by seeding pacemaker cells on appropriate scaffolds in vitro.<sup>(11)</sup>

Today, bone mesenchymal stem cells appear to be optimal for the biological transformation of pacemaker cells.

### **Clinical applications of stem cell therapy in angiology**

One action of stem cells that contributes to tissue regeneration is the increase in vascularization of damaged tissue. The supply of stem cells can influence the release of various angiogenic factors and cytokines or provide endothelial cell progenitors capable of acting directly on the angiogenic mechanism. Precisely, stem cell transplantation in angiology is performed based on this action.<sup>(4)</sup>

We can affirm that autologous transplantation of stem cells from peripheral blood (CMN-SP) is considered a new therapeutic angiogenesis strategy that is very useful and effective in critical ischemia of the lower limbs. Likewise, the favorable results of PCM injection in patients with chronic lower limb lymphedema are very encouraging. A progressive decrease in the diameter of the injected limb is achieved, even in the lower limb where the cell implant is not performed. The improvement is evident between 3 and 6 months after implantation, with a reduction in fibroadenoma, improvement in trophic changes, a decrease in the frequency of lymphangitis, and the disappearance of pain. These results support the criterion that some bone marrow-derived cells may be involved in lymphangiogenesis.

The positive results of BMN autotransplantation in diabetic patients with skin ulcers in the lower limbs are remarkable. In these patients, the therapeutic response is effective, as histologically, granulation tissue and valuable epithelialization for secondary healing, abundant newly formed vessels, and cells that promote faster fibrosis and healing are observed.<sup>(4)</sup>

Post-phlebotic or post-thrombotic syndrome is simply the main sequela of venous thrombosis of the lower limbs, which is caused by significant venous stasis due to valve destruction. One therapeutic alternative for these patients has been the implementation of regenerative cell therapy. The results obtained so far are encouraging.<sup>(4)</sup>

### **Clinical applications of stem cell therapy in ophthalmology**

Stem cell therapy has been widely used in this specialty in diseases that compromise the corneal limbus,

such as limbal insufficiency due to extrinsic factors such as inflammatory processes or cicatricial pemphigoid, Steven Johnson syndrome, due to the use of drugs such as mitomycin and 5-fluorouracil, or intrinsic conditions such as congenital aniridia and idiopathic limbal insufficiency.<sup>(12)</sup>

In current regenerative medicine, one of the priorities is to improve the biointegration of these prostheses by facilitating their colonization by epithelial cells and neurons. Growth factors such as EFG improve the proliferation and migration of epithelial cells on the prostheses, while TGF- $\beta$  appears to prevent the formation of membranes on the inner surface of the prosthesis.<sup>(12)</sup>

The treatment of retinitis pigmentosa is a highly debated topic. In Cuba, 90 patients have already been treated with autologous mobilized CMN-SPs injected by various routes, including intravitreal and intravenous. The results are very encouraging, with no significant adverse effects. To our knowledge, Cuba is one of only two countries using this therapeutic method.<sup>(12)</sup>

### **Clinical applications of stem cell therapy in neurology**

Incurable neurological diseases have always been one of the main problems to be solved by researchers. These diseases, such as Alzheimer's, Parkinson's, and Huntington's disease, are usually treated with drugs that, in most cases, end up with unfavorable results and are even worse for patients; for this reason, cell therapy offers an alternative to these diseases. Implementing stem cells allows these patients to renew or generate neuronal cells.<sup>(13)</sup>

We believe that stem cells are required in Parkinson's disease to regenerate cells capable of synthesizing and releasing dopamine.

The use of embryonic stem cells as a source of dopaminergic neurons for the treatment of Parkinson's disease is a prospect of growing interest. There is evidence that dopaminergic neurons derived from embryonic stem cells survive for extended periods of time (more than 37 weeks).<sup>(13)</sup>

The therapeutic potential of mesenchymal stem cells has also been examined in patients with Parkinson's disease, and the intrinsic neuro-restorative capacity of mesenchymal stem cells and their usefulness as a source of dopaminergic neurons has been evaluated.<sup>(13)</sup>

Cell therapy has also been used in other nervous system disorders, including amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS). In eight cases of ALS in Cuba, intravenous administration of autologous mobilized MSCs also provided some clinical improvement, except in patients with bulbar involvement. It has been suggested that acupuncture with stem cell application may be an effective regenerative treatment.<sup>(14)</sup>

We have also documented that intracerebral injection of umbilical cord-derived mesenchymal stem cells in patients with Alzheimer's disease reduces the expression of markers of glial activation, oxidative stress, and apoptosis in their brains, which is accompanied by a recovery of learning ability and memory performance in these individuals.

Intravenous injection of bone marrow-derived mesenchymal stem cells in a patient with Alzheimer's disease revealed, for the first time, the ability of these cells to migrate to the brain and a reduction in the size of amyloid pE3-A $\beta$  plaques. It has also been reported that the administration of mesenchymal stem cells in Alzheimer's patients significantly increases hippocampal neurogenesis and the differentiation of neural progenitors into mature neurons. This result may have a significant impact on future strategies for the treatment of Alzheimer's disease.<sup>(14)</sup>

### **Clinical applications of stem cell therapy in gastroenterology**

Combining cell and gene therapy using genetically modified MMC could represent a new therapeutic tool for treating liver cirrhosis.<sup>(15)</sup>

MMC transplantation reduces the expression and production of type I and III collagen, the expression of pro-fibrogenic cytokines such as TGF- $\beta$ 1,  $\alpha$ -SMA, and TNF- $\alpha$ , and the activation of HE cells; at the same time, it reduces apoptosis and stimulates hepatocyte proliferation and angiogenesis.<sup>(15)</sup>

### **Clinical applications of stem cell therapy in orthopedics**

Osteoarticular disorders have undoubtedly been the most studied in regenerative medicine and are among those with the most clinical evidence. Compared to the current gold standard of autologous bone block grafting in fractures with bone loss, stem cells mixed with demineralized bone and platelet-rich plasma are superior and reduce repair time by half. There is also sufficient evidence that intra-articular injection of stem cells with growth factors in osteoarthritis results in clear recovery of cartilage and clinical parameters (pain and functional limitation), arthroscopic parameters, and quality of life. Studies show that the optimal response in disc degeneration is several times higher than in patients treated without regenerative medicine.<sup>(16)</sup>

Cell therapy has proven very promising and safe in patients treated in Cuba with orthopedic or traumatic conditions. Rapid regeneration of bone cysts and a good evolution of pseudoarthrosis have been observed. The results obtained in treating knee osteoarthritis open up excellent prospects.<sup>(16)</sup>



### **Clinical applications of stem cell therapy in traumatology**

This therapy has been used in different diseases in which treatment has not been as successful as expected, for example, significant bone defects, osteonecrosis, fracture union failure, osteoarthritis, and tendon rupture. Generally, the most frequently used sources of adult stem cells are bone marrow and adipose tissue.<sup>(16)</sup>

Various applications have been carried out in traumatology using stem cells, which have shown promising results, such as in the treatment of long bone defects, fractures, cartilage regeneration, and tendon regeneration. Stem cells are also used in the treatment of osteonecrosis, as necrotic tissue has poor osteoprogenitor cells.<sup>(16)</sup>

### **Clinical applications of stem cell therapy in pulmonology**

Today, there are treatments based on hematopoietic stem cells (derived from bone marrow) and mesenchymal stem cells (obtained mainly from adipose tissue) that have demonstrated their therapeutic usefulness in respiratory diseases, thanks to their regenerative potential since they are capable of differentiating into various types of tissues, and their ability to promote the release of anti-inflammatory factors, reducing the progression of lung damage.<sup>(17)</sup>

In Cuba, a 9-year-old boy with idiopathic pulmonary fibrosis who was indicated for lung transplantation was treated. Autologous CMN-MO was administered orotracheally. There was a progressive improvement, and the stated transplantation was avoided. This result demonstrated cell therapy's potential for treating pulmonary fibrosis and other chronic lung diseases.<sup>(2)</sup>

Stem cell transplantation is an up-and-coming method for treating inflammatory lung diseases, including COPD. It could help improve the signs and symptoms of this disease, such as shortness of breath, especially during physical activity, wheezing, chest tightness, excess mucus in the lungs, chronic cough, frequent respiratory infections, lack of energy, swelling in the ankles, feet, or legs, and cyanosis or blue discoloration of the lips and nails.<sup>(18)</sup>

### **Clinical applications of stem cell therapy in dermatology**

The therapeutic potential of stem cells has been explored with varying results in various skin diseases. Stem cell therapy has become a new strategy for facial rejuvenation and filling unwanted wrinkles and expression lines, removing scars and acne marks, augmenting and beautifying breasts and buttocks, and post-mastectomy breast reconstruction, among other things.<sup>(2)</sup>

Mesenchymal stem cells are used positively in burns and skin lesions secondary to radiotherapy, where epithelial regeneration, angiogenesis, and significant tissue hydration have been demonstrated. The use of MSCs in the treatment of chronic wounds has multiple objectives: to accelerate tissue repair, to cushion inflammatory events, and to reduce or eliminate scar formation.<sup>(19)</sup>

Research into the usefulness of MSCs in treating alopecia is booming; however, there are currently no data demonstrating their clinical efficacy.<sup>(20)</sup>

Autologous transplants of mixed melanocyte and keratinocyte cell cultures have been used to treat vitiligo, as the interactions between these cells increase the proliferation and migration of melanocytes.<sup>(20)</sup>

### **Clinical applications of stem cell therapy in nephrology**

Currently, the main areas for scientific research with stem cells in nephrology are tissue repair, paracrine and endocrine actions, and organogenesis. Studies on renal tissue can cite glomerular repair and tubular injury, grafting in damaged nephrons and acute kidney injury (AKI), and chronic degenerative diseases such as chronic kidney disease (CKD) and diabetic nephropathy.<sup>(21)</sup>

### **Cell therapy in endocrinology**

Recent studies showing positive results from pancreatic islet transplantation in diabetic patients have increased interest in using cells capable of producing insulin. The possibility of using stem cells with the ability to differentiate into insulin-producing cells would be a much more attractive strategy.

Similarly, various studies suggest that cells obtained from the liver, pancreatic ducts, pancreatic islets, or even bone marrow can produce insulin-secreting cells.

### **Clinical applications of stem cell therapy in hematology**

Stem cell transplantation may be part of the treatment of blood disorders (such as leukemia), some types of lymphoma (including Hodgkin's disease), aplastic anemia, thalassemia, sickle cell disease (sickle cell anemia or sickle cell disease), and some metabolic disorders or congenital immunodeficiencies (such as chronic granulomatous disease).<sup>(8)</sup>

### **Clinical applications of stem cell therapy in oncology**

Occasionally, stem cell transplants can be used to replace bone marrow cells that have been destroyed

during the treatment of cancers of organs such as breast cancer or neuroblastoma.<sup>(8)</sup>

In addition to replacing cells damaged by chemotherapy or disease, stem cells serve to strengthen the donor's immune system and fight certain types of cancer and blood-related diseases, such as leukemia, lymphoma, neuroblastoma, and multiple myeloma.<sup>(22)</sup>

### **Stem cell therapy as an alternative to treatment and rehabilitation for patients with COVID-19**

The world is working around the clock to find a treatment for COVID-19. Cell therapy is one possible therapeutic strategy that will enable us to tackle this disease triggered by SARS-CoV-2. Stem cells are one of the alternatives that researchers are focusing on.<sup>(23)</sup>

The inflammatory component plays a vital role throughout this disease, and given the high anti-inflammatory power demonstrated by mesenchymal stromal stem cells *in vivo* and *in vitro*, many researchers have opted for this line as a therapeutic alternative to COVID-19. Spanish research groups have played and continue to play a very active role, and five clinical trials are currently underway for treating coronavirus with cell therapy. There are currently 29 clinical trials of cell therapy against coronavirus underway worldwide. There is already evidence of the good results of these therapies in treating patients with moderate to severe disease, with improvements in their respiratory and radiological parameters. Advanced therapies, and in this case, cell therapy, are positioned as therapeutic tools that will help shape future medicine.<sup>(23)</sup>

Mesenchymal cells play an important role, mainly through two pathways: their immunomodulatory properties and anti-inflammatory capacity. These cells are capable of secreting many cytokines in a paracrine manner or can interact through direct contact with immune system cells, including T and B lymphocytes, dendritic cells, macrophages, and NK cells, thus achieving immunomodulation.<sup>(24)</sup>

Multiple studies have examined the use of mesenchymal stem cells derived from fat (MSCs) in the treatment of lung disease.<sup>(25)</sup>

The first case of COVID-19 treated with mesenchymal cells obtained from the umbilical cord was in China. In this country, a study was conducted in which stem cells were injected intravenously into the bloodstream of seven seriously ill patients. The treatment was successful in all seven patients who were discharged from the hospital within 14 days.<sup>(24)</sup>

This study has shown that intravenous administration of certain types of human mesenchymal stem cells is a safe and effective method for treating patients with COVID-19, even those who are elderly and have severe pneumonia.<sup>(26)</sup>

The study conducted by the company Pluristem, using placental MSCs in seven patients confirmed with COVID-19, showed encouraging clinical results

This protocol will be extended to the United States under FDA supervision. In addition, the Miller School of Medicine, University of Miami, United States, initiated a clinical trial with intravenous umbilical cord MSCs in 24 patients with confirmed COVID-19 complications.<sup>(27)</sup>

We have shown that current MSC therapies have shown positive results in clinical and animal studies. Treatment with MSCs as adjuvant therapy for COVID-19 patients may influence clinical and radiological lung evolution, control the inflammatory-immune cascade, facilitate alveolar regeneration, and ultimately control or reduce pulmonary fibrosis.

This procedure is also being applied for the first time in Cuba for post-pandemic injuries. The method consists of the intravenous administration of a stem cell concentrate that includes hematopoietic cells and others with immunoregulatory properties, which reduce or stop the residual interstitial inflammatory process that caused the viral infection and, as a result, the recovery of damaged tissue. This stem cell therapy was applied to eight patients in Havana with satisfactory results.

In Villa Clara, stem cell treatment led to a favorable recovery in Yaquelin Collado, a patient with COVID-19. After being admitted to the Comandante Manuel Fajardo Hospital in this city for 59 days, 37 of them in intensive care, the patient was discharged on May 22, 2020, and two months later, she began treatment with regenerative medicine. This method of replacing damaged cells with healthy cells was explicitly used in the patient after she presented with lung damage caused by SARS-CoV-2, the cause of the disease. After six months, the repair, restoration, and regeneration of cells, tissues, and organs were verified, and a favorable recovery was observed.<sup>(28)</sup>

### **CONCLUSIONS**

A comprehensive evaluation of the information presented above leads to the conclusion that regenerative cell therapy with stem cells constitutes a broad universe with effective therapeutic potential for various medical specialties. This therapy is also applicable to treating and rehabilitating patients diagnosed with COVID-19. This therapy offers excellent alternatives to treating multiple health conditions, often with results superior to conventional treatments.

## **BIBLIOGRAPHICAL REFERENCES**

1. Ruiz Navarro F. Orígenes de la medicina regenerativa. [Internet]. 2020. [citado 2021 Ago 02]: [aprox. 3 p.]. Disponible en: [https://www.regmedaustria.org/images/Allg.Infos\\_Literatur/Literature-4ParaHispanoparlantes-OrigenesDeLaMedicinaRegenerativa.pdf](https://www.regmedaustria.org/images/Allg.Infos_Literatur/Literature-4ParaHispanoparlantes-OrigenesDeLaMedicinaRegenerativa.pdf)
2. Isaza CA. La medicina regenerativa: fundamentos y aplicaciones. [Internet]. 2018. [citado 2021 Ago 02]: [aprox. 6 p.]. Disponible en: <http://www.scielo.org.co/pdf/rmri/v24n2/0122-0667-rmri-24-02-119.pdf>
3. Roque Pérez L, Flores González CA, López Berrio S. A propósito del artículo “Desarrollo de la medicina regenerativa en Cuba”. MediCiego [Internet]. 2018 [citado 2021 Ago 16], 24(4): [aprox. 2 p.]. Disponible en: <http://www.revmediciego.sld.cu/index.php/mediciego/article/view/1170>
4. Pérez L, Yaisel Alfonso Y, Plaín Pazos C. Aplicaciones de las células madre en la angiología cubana. MediCiego [Internet]. 2018 [citado 2021 Ago 16], 24(4): [aprox. 6 p.]. Disponible en: <https://dialnet.unirioja.es/servlet/articulo?codigo=7079868>
5. Vidal Ramos B. Beneficiados más de cuatro mil pacientes con la medicina regenerativa. [Internet]. 2016. [citado 2021 Ago 02]: [aprox. 2 p.]. Disponible en: <https://www.telecubanacan.icrt.cu/provinciales/beneficiados-mas-de-cuatro-mil-pacientes-con-la-medicina-regenerativa/>
6. Colectivo de autores. Células madre. Generalidades (Parte I). Hospital General Provincial Docente “Dr. Antonio Luaces Iraola” Ciego de Ávila. [Internet]. 2016 [citado 2021 Ago 22]: [aprox. 15 p.]. Disponible en: <http://www.revmediciego.sld.cu>
7. Hertl, Martin. Trasplante de células madre. [Internet]. 2019 [citado 2021 Ago 22]: [aprox. 5 p.]. Disponible en: <https://www.rushu.rush.edu/faculty/martin-hertl-md-phd-facs>
8. Colectivo de autores. Trasplante celular y terapia regenerativa con células madre. Anales Sistema Sanitario de Navarra vol.29 supl.2 Pamplona may./ago. 2006. [Internet]. 2006 [citado 2021 Ago 22]: [aprox. 13 p.]. Disponible en: [https://scielo.isciii.es/scielo.php?script=sci\\_serial&pid=1137-6627&lng=es&nrm=iso](https://scielo.isciii.es/scielo.php?script=sci_serial&pid=1137-6627&lng=es&nrm=iso)
9. Riverón Cruzata LJ, Morales Álvarez L, Gutiérrez Carbonell AM, Cruz EM, Barreda Pavón JL, Rojas Pérez S. Terapia celular en el infarto del miocardio. [Internet]. 2017 Abr [citado 2021 Ago 02]; 56 (266): [aprox. 7 p.]. Disponible en: <https://www.semanticscholar.org/paper/Terapia-celular-en-el-infarto-agudo-de-miocardio-Sánchez-Fernández-Avilés/8549526e5b8964fcaec821056d9782facdaaf774?p2df>
10. Ayala Lugo A. Medicina regenerativa y enfermedades cardiovasculares: Terapia con células madre. [Internet]. 2007 Dic [citado 2021 Ago 02]; 5(2): [aprox. 4 p.]. Disponible en: <http://archivo.bc.una.py/index.php/RIIC/article/view/323>
11. Martínez de Hoyo K, Ortega Enciso A, Mendoza Beltrán F, Reynolds Pombo J. Células madre como alternativa al marcapaso intravenoso. Rev. Col. Cardio. Internet]. 2020 [citado 2021 Ago 02]; 27 (4): [aprox. 8 p.]. Disponible en: <https://doi.org/10.1016/j.rccar.2019.09.017>. <https://www.sciencedirect.com/science/article/pii/S0120563319302153>
12. Parapar Tena SI, Cambas Andreu AA, Cueto Samada D, Pérez Marrero MJ. Suero autólogo ¿Medicina regenerativa en oftalmología? Rev. Calixto. [Internet]. 2018 [citado 2021 Ago 02]; 6 (1): [aprox. 9 p.]. Disponible en: <http://revcalixto.sld.cu/index.php/ahcg/article/view/188>
13. García Y, González R, Rangel F, Torres V. Células madre como tratamiento regenerativo para la enfermedad de Parkinson. Rev. Vive. [Internet]. 2019 [citado 2021 Ago 02]; 2(6): 134-143. <https://doi.org/10.33996/revistavive.v2i6.34>
14. López León M, Lehmann M, G. Goya R. Medicina regenerativa para el tratamiento de enfermedades neurodegenerativas. [Internet]. 2017 [citado 2021 Ago 02]: [aprox. 5 p.]. Disponible en: [https://www.inibiop.org.ar/Descargas/Publicaciones\\_Goya\\_PDF/LLeon-2016%20Murcia.pdf](https://www.inibiop.org.ar/Descargas/Publicaciones_Goya_PDF/LLeon-2016%20Murcia.pdf)
15. Fiore EJ; Picazo E; Aquino JB, Mazzolini Rizzo GD. Células Madre Mesenquimales y Medicina Regenerativa en la Cirrosis Hepática. [Internet]. 2017 [citado 2021 Ago 02]; 77(6): [aprox. 7 p.]. Disponible en: <http://www.https://doi.org/10.56294/ri2026181>



16. Vélez R. Medicina regenerativa, terapia células madre. [Internet]. 2020 [citado 2021 Ago 02]: [aprox. 5 p.]. Disponible en: <https://dialnet.unirioja.es/servlet/dctes?codigo=118683>
17. Tello Vera S. Fibrosis pulmonar idiopática tratada con células madres mesenquimales alogénicas derivadas de tejido adiposo. Reporte de caso. Rev. Cuerpo Médico Del HNAAA. [Internet]. 2019 [citado 2021 Ago 17]; 11(4): 250 - 252. Disponible en: <https://doi.org/10.35434/rcmhnaaa.2018.114.468>
18. Silva O R, Montes JF, García Valero J, Olloquequi J. Efectores celulares de la respuesta inflamatoria en la enfermedad pulmonar obstructiva crónica. Rev. méd. Chile [Internet]. 2015 Sep [citado 2021 Ago 17]; 143(9): 1162-1171. Disponible en: [http://www.scielo.cl/scielo.php?script=sci\\_arttext&pid=S0034-98872015000900009&lng=es](http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0034-98872015000900009&lng=es)
19. Socarrás Ferrer BB, del Valle Pérez LO, de la Cuétara Bernal K, et al. Células madre mesenquimales: aspectos relevantes y aplicación clínica en la medicina regenerativa. Rev Cubana Hematol Inmunol Hemoter. [Internet]. 2017 [citado 2021 Ago 17]; 29(1):16-23. Disponible en: [http://scielo.sld.cu/scielo.php?script=sci\\_arttext&pid=S086402892013000100003&lng=es](http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S086402892013000100003&lng=es)
20. Blasco Morente G, Arias Santiago S. Aplicaciones de células madre en dermatología. [Internet]. 2016 [citado 2021 Ago 17]; 22(4): [aprox. 4 p.]. Disponible en: <https://dialnet.unirioja.es/servlet/articulo?codigo=4654885>
21. Suller Garcia J, Aparecida Reis L, Parisio de Abreu N, Schor N. Células madre en Nefrología. [Internet]. 2016 [citado 2021 Ago 17]: [aprox. 4 p.]. Disponible en: [https://www.google.com/url?sa=t&source=web&rct=j&url=https://redemc.net/campus/wp-content/uploads/2015/08/M1-C%25C3%25A9lulas-madre-en-nefrolog%25C3%25ADa-Nestor-Schor-ESP.pdf%3FxFx20542&ved=2ahUKEwiVyPW08M\\_wAhWiaDABHby\\_C18QFjAAegQIAxAC&usg=AOvVaw2-L9I2PXrttfi499laDvmW](https://www.google.com/url?sa=t&source=web&rct=j&url=https://redemc.net/campus/wp-content/uploads/2015/08/M1-C%25C3%25A9lulas-madre-en-nefrolog%25C3%25ADa-Nestor-Schor-ESP.pdf%3FxFx20542&ved=2ahUKEwiVyPW08M_wAhWiaDABHby_C18QFjAAegQIAxAC&usg=AOvVaw2-L9I2PXrttfi499laDvmW)
22. Mayo Clinic. Células madre: qué son y qué hacen. June 08, 2019. [Internet]. 2019 [citado 2021 Ago 22]: [aprox. 14 p.]. Disponible en: <https://www.mayoclinic.org/es-es/about-this-site/welcome>
23. Suárez P. Células madre para el tratamiento del coronavirus. [Internet]. 2020 [citado 2021 Ago 17]: [aprox. 1 p.]. Disponible en: [https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.institutoche.es/observatorio/firmasalla/celulas\\_madre\\_para\\_el\\_tratamiento\\_del\\_coronavirus&ved=2ahUKEwjR9qzG8M\\_wAhVmQjABHbKOC14QtwlwAHoECAMQAg&usg=AOvVaw0hxOHuo9hUUVLvCytRMxPyP](https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.institutoche.es/observatorio/firmasalla/celulas_madre_para_el_tratamiento_del_coronavirus&ved=2ahUKEwjR9qzG8M_wAhVmQjABHbKOC14QtwlwAHoECAMQAg&usg=AOvVaw0hxOHuo9hUUVLvCytRMxPyP)
24. López LJC, Acosta BC, López NJC. Actualización sobre COVID-19 y posible manejo de sus complicaciones sistémicas graves con células troncales mesenquimales. Rev Mex Cir Bucal Maxilofac. [Internet]. 2020 [citado 2021 Ago 17]; 16(2-3): 61-70. Disponible en: [https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.medigraphic.com/cgi-bin/new/resumen.cgi%3FIDARTICULO%3D97703&ved=2ahUKEwjxITVkJ9LwAhUqUt8KHRQuDNsQFjAAegQIBBAC&usg=AOvVaw2\\_dzpNRC6Knw7pjks5UDNF](https://www.google.com/url?sa=t&source=web&rct=j&url=https://www.medigraphic.com/cgi-bin/new/resumen.cgi%3FIDARTICULO%3D97703&ved=2ahUKEwjxITVkJ9LwAhUqUt8KHRQuDNsQFjAAegQIBBAC&usg=AOvVaw2_dzpNRC6Knw7pjks5UDNF)
25. Centurion Rivas P, De La Cruz Vargas JA, Llanos Tejada F, Talavera E, Delgado M. Células madre mesenquimales (MSC) fotoestimuladas, derivadas de la grasa: Enfoque terapéutico adyuvante del síndrome respiratorio agudo y preventivo de la fibrosis pulmonar en COVID-19. [Internet]. 2020 [citado 2021 Ago 22]: [aprox. 1 p.]. Disponible en: <https://repositorio.urp.edu.pe/bitstream/handle/URP/3034/CE%CC%81LULAS%20MADRE%20MESENQUIMALES.pdf?sequence=2&isAllowed=y>
26. Hernández Perera JC. Células madre para combatir la COVID-19. [Internet]. 2020 [citado 2021 Ago 17]; 11(2): 216-28. Disponible en: [https://www.google.com/url?sa=t&source=web&rct=j&url=https://files.sld.cu/cimeq/files/2020/05/Bol-CCimeq-2020-1-5-pag5.pdf&ved=2ahUKEwixqlql8M\\_wAhWiQjABHUo4DI8QFjAAegQIAxAC&usg=AOvVaw2y4fRvtXSnXoeV1i1AMCVk](https://www.google.com/url?sa=t&source=web&rct=j&url=https://files.sld.cu/cimeq/files/2020/05/Bol-CCimeq-2020-1-5-pag5.pdf&ved=2ahUKEwixqlql8M_wAhWiQjABHUo4DI8QFjAAegQIAxAC&usg=AOvVaw2y4fRvtXSnXoeV1i1AMCVk)
27. Fernández Salazar JA. Cuba aplica terapia regenerativa para tratar a pacientes recuperados de la COVID-19. [Internet]. 2020 [citado 2021 Ago 17]: [aprox. 3 p.]. Disponible en: <https://www.eldiariodesantiagodecuba.com/cuba-aplica-terapia-regenerativa-para-tratar-a-pacientes-recuperados-de-la-covid-19-foto-y-video/>
28. Falcón F. Tratamiento con células madres recupera paciente con COVID-19 en Cuba. [Internet]. 2020

[citado 2021 Ago 17]: [aprox. 6 p.]. Disponible en: <http://www.trabajadores.cu/20210130/tratamiento-con-celulas-madres-recupera-paciente-con-covid-19-en-cuba-fotos/>

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None.

#### CONFLICT OF INTERESTS

None.

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